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Sustained Release of the HIV Microbicides Maraviroc and Emtricitabine from Modified Silicone Elastomer Vaginal Gels

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Purpose

Silicone elastomer gels (SEGs), consisting of lightly crosslinked polydimethylsiloxane (ST-Elastomer 10) and cyclomethicone, are commonly used in a range of cosmetic applications and are currently being developed for topical drug delivery applications. Recently, SEGs have been shown to provide sustained pharmacokinetics of the HIV entry inhibitor maraviroc (MVC) following vaginal administration in macaques. The objective of this study was to evaluate a range of second generation SEGs wherein the cyclomethicone component of the gel has been replaced with a low molecular weight (MW) hydroxyl-terminated, linear polydimethylsiloxane (h-PDMS). We anticipated that the resulting hydrophilic h-SEGs would offer enhanced release rates for HIV microbicide candidates MVC and emtricitabine (FTC) compared to conventional SEGs.

Methods

Continuous flow rheology was performed on h-SEGs prepared with different MW h-PDMS. In vitro release testing was performed on viscosity-matched gels containing either 5% w/w MVC or FTC in both simulated vaginal fluid (SVF) and a solvent/water system. Solubilities of MVC and FTC were determined in different MW h-PDMS.

Results

The viscosity of h-SEGs increased with ST-Elastomer 10 concentration. h-SEG gel compositions, viscosity-matched to a conventional 80:20% w/w SEG and a 2.2% w/w HEC gel (~50Pa.S), were chosen for in vitro release testing. Release of MVC and FTC from a low MW h-SEG was significantly increased in both dissolution media ((MVC; 18mg (SVF), 21mg (IPA/water), FTC; 4mg (SVF), 14mg (IPA/water)) compared to the conventional SEG gel (MVC; 3 mg (SVF), 12 mg (IPA/water), FTC; 2 mg (SVF), 9mg (IPA/water)). Release from high MW h-SEGs was comparable to the conventional SEG gel in both media. Solubility of MVC and FTC in the low MW h-PDMS (MVC; 40mg/mL, FTC; 0.4mg/mL) was significantly greater than in cyclomethicone (MVC; <5µg/mL, FTC; <1.1µg/mL).

Conclusion

The results demonstrated that SEG hydrophilicity can be readily modified by substituting the cyclomethicone component of the elastomer gel with low MW h-PDMS. Increasing the proportion of hydroxyl groups significantly enhanced release and solubility of both model hydrophobic (MVC) and hydrophilic (FTC) microbicides compared to the conventional SEG. The results highlight the potential of these second generation SEGs for vaginal delivery of HIV microbicides.